ABSTRACT

Vaccine development for squamous cell carcinoma of the head and neck (SCCHN) is the major research objective of our laboratories. Based on extensive prior studies in animal models and ex vivo in patients, we now propose to perform a Phase I clinical trial for up to 24 patients with SCCHN (AJCC Stage II/IV), using a novel DNA-based vaccination strategy. The vaccine is prepared by transferring DNA from the patient's neoplasm into highly immunogenic nonmalignant human fibroblasts where genes specifying tumor-associated antigens (TAAs) are expressed. The fibroblasts free of adventitious infectious agents and lethally irradiated (10,000 cGy) before immunization, express both allogeneic and syngeneic class I MHC determinants (HLA A-2). This type of vaccine is based on the principle that TAAs are the products of mutated/dysregulated genes in the cancer cells, which differ from the homologous genes in nonmalignant cells of the patient. Genes specifying weakly immunogenic TAAs transferred from the patient's neoplasm into the fibroblasts are stably expressed. Our prior data in murine models indicate that immunization with such DNA-based vaccines induces robust, specific anti tumor immune responses and immunologic memory, leading to tumor rejection. After completion of conventional therapy, patients with SCCHN will receive a series of immunizations with autologous tumor-DNA-transfected cells. The primary endpoint is safety and toxicity of immunization. Secondary endpoints are the induction and evaluation of the immune response against autologous tumor. A master bank of human fibroblasts will be prepared and tested for contamination with adventitious infectious agents. The cells will serve as recipients of DNA derived from each patient's neoplasm. After transfection, the number of modified cells will be increased, lethally irradiated and delivered as a vaccine. Patients will be monitored by ELISPOT-interferon g assays both before and after immunization for the frequency of tumor-specific CD8+ and CD4+ T cells in the peripheral blood. Additional immune monitoring studies will be performed to determine if immunosuppressive effects of the patient's cancer were modified by the immunizations. It is expected that the vaccine, which combines known requirements for generation of anti tumor immune responses, (improved TAA expression and allogeneic stimulation) will be of benefit to patients with squamous cell carcinoma of the head and neck.

Performance sites
University of Illinois College of Medicine, Chicago, Illinois
University of Chicago, Chicago, Illinois
University of Pittsburgh Cancer Institute, Pittsburgh, Pennsylvania

Key personnel
Edward P. Cohen, MD
University of Illinois
Principal Investigator

Theresa L. Whiteside, PhD
University of Pittsburgh
Co-Principal Investigator